****

Reviewer Comments:

<210> 2

<211> 1776

<212> DNA

<213> Artificial Sequence

<220>

<223> modified NS5B

(ERRORED PORTION SHOWN BELOW)

<221> variation

<222> (83)...(83)

<223> n = G or T

tcnatgtcnt acncntggac nggngccntn atnacaccat gtgggcccga agaggagaag 60

ttaccgatca nccctctgag taattcgctc atncggttcc ataataaggt gtactccaca 120

The above "<220>-<223>" section describing the "n" at location 83 is errored: "a" is at that location. The "n" at location 93 is not explained above.

<210> 4

<211> 4182

<212> DNA

<213> Artificial Sequence

<220>

<223> modified NS3-5A

<221> variation
<222> (2711)...(2711)
<223> n = T or C

<221> variation
<222> (3645)...(3645)
<223> n = A or G

(ERRORED PORTIONS SHOWN BELOW)

gtgggtccgg gagagggggc tgtgcagtgg atgaaccggc tgatagcgtt cgcctcgcgg 2700
ggtaatcatg tttcccccac gcactatgtg cctgagagcg acgccgcagc gcgtgttact 2760

There is no "n" at location 2711: "t" is at that location.

ttgtctgcgc cttccttgaa ggcgacatgc actacccacc atgtctctcc ggacgctgac 3600
ctcatcgagg ccaacctcct gtggcggcag gagatgggcg ggancatcac ccgcgtggag 3660

There is no "n" at location 3645: "c" is at that location. The "n" at
location 3644 is not explained above.
****

Validated By CRFValidator v 1.0.3

Application No: 10577893   Version No: 1.0

Input Set:

Output Set:

Started: 2011-03-11 10:24:53.976
Finished: 2011-03-11 10:24:56.181
Elapsed: 0 hr(s) 0 min(s) 2 sec(s) 205 ms
Total Warnings: 28
Total Errors: 2
No. of SeqIDs Defined: 28
Actual SeqID Count: 28

Error code	Error Description
W 213	Artificial or Unknown found in <213> in SEQ ID (1)
W 213	Artificial or Unknown found in <213> in SEQ ID (2)
E 342	'n' position not defined found at POS: 93 SEQID(2)
W 213	Artificial or Unknown found in <213> in SEQ ID (3)
W 213	Artificial or Unknown found in <213> in SEQ ID (4)
E 342	'n' position not defined found at POS: 3644 SEQID(4)
W 213	Artificial or Unknown found in <213> in SEQ ID (5)
W 213	Artificial or Unknown found in <213> in SEQ ID (6)
W 213	Artificial or Unknown found in <213> in SEQ ID (7)
W 213	Artificial or Unknown found in <213> in SEQ ID (8)
W 213	Artificial or Unknown found in <213> in SEQ ID (9)
W 213	Artificial or Unknown found in <213> in SEQ ID (10)
W 213	Artificial or Unknown found in <213> in SEQ ID (11)
W 213	Artificial or Unknown found in <213> in SEQ ID (12)
W 213	Artificial or Unknown found in <213> in SEQ ID (13)
W 213	Artificial or Unknown found in <213> in SEQ ID (14)
W 213	Artificial or Unknown found in <213> in SEQ ID (15)
W 213	Artificial or Unknown found in <213> in SEQ ID (16)
W 213	Artificial or Unknown found in <213> in SEQ ID (17)
W 213	Artificial or Unknown found in <213> in SEQ ID (18)

Input Set:

Output Set:

Started:	2011-03-11 10:24:53.976
Finished:	2011-03-11 10:24:56.181
Elapsed:	0 hr(s) 0 min(s) 2 sec(s) 205 ms
Total Warnings:	28
Total Errors:	2
No. of SeqIDs Defined:	28
Actual SeqID Count:	28

Error code	Error Description
W 213	Artificial or Unknown found in <213> in SEQ ID (19)
W 213	Artificial or Unknown found in <213> in SEQ ID (20) This error has occured more than 20 times, will not be displayed

<110> Ludmerer, Steven W.

     Graham, Donald J.

     LaFemina, Robert L.

     Flores, Osvaldo A.

     Pizzuti, Maura

     Traboni, Cinzia

<120> HCV REPLICONS CONTAINING NS5B FROM
  GENOTYPE 2B

<130> 21564YP

<140> 10577893
<141> 2011-03-11

<150> PCT/US2004/036575
<151> 2004-11-03

<150> 60/517,605
<151> 2003-11-05

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 591
<212> PRT
<213> Artificial Sequence

<220>
<223> modified NS5B

<221> VARIANT
<222> (5)...(5)
<223> Xaa = threonine or serine

<221> VARIANT
<222> (24)...(24)
<223> Xaa = asparagine or serine

<221> VARIANT
<222> (31)...(31)
<223> Xaa = methionine or isoleucine

<221> VARIANT
<222> (392)...(392)
<223> Xaa = isoleucine or leucine

<400> 1
Ser Met Ser Tyr Xaa Trp Thr Gly Ala Leu Ile Thr Pro Cys Gly Pro
 1   5   10   15
Glu Glu Glu Lys Leu Pro Ile Xaa Pro Leu Ser Asn Ser Leu Xaa Arg

```
                 20                    25                    30
Phe His Asn Lys Val Tyr Ser Thr Thr Ser Arg Ser Ala Ser Leu Arg
         35                    40                    45
Ala Lys Lys Val Thr Phe Asp Arg Val Gln Val Leu Asp Ala His Tyr
    50                    55                    60
Asp Ser Val Leu Gln Asp Val Lys Arg Ala Ala Ser Lys Val Ser Ala
65                    70                    75                    80
Arg Leu Leu Thr Val Glu Glu Ala Cys Ala Leu Thr Pro Pro His Ser
                 85                    90                    95
Ala Lys Ser Arg Tyr Gly Phe Gly Ala Lys Glu Val Arg Ser Leu Ser
                 100                   105                   110
Arg Arg Ala Val Asn His Ile Arg Ser Val Trp Glu Asp Leu Leu Glu
         115                   120                   125
Asp Gln His Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val
    130                   135                   140
Phe Cys Ile Asp Pro Thr Lys Gly Gly Lys Lys Pro Ala Arg Leu Ile
145                   150                   155                   160
Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr
                 165                   170                   175
Asp Ile Ala Gln Lys Leu Pro Lys Ala Ile Met Gly Pro Ser Tyr Gly
         180                   185                   190
Phe Gln Tyr Ser Pro Ala Glu Arg Val Asp Phe Leu Leu Lys Ala Trp
         195                   200                   205
Gly Ser Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe
    210                   215                   220
Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr
225                   230                   235                   240
Gln Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu
                 245                   250                   255
Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Thr Asn Ser Lys Gly Gln
         260                   265                   270
Ser Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser
         275                   280                   285
Met Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys
    290                   295                   300
Ala Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu
305                   310                   315                   320
Val Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu
                 325                   330                   335
Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
         340                   345                   350
Leu Pro Arg Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
         355                   360                   365
Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Arg Tyr Phe Leu
    370                   375                   380
Thr Arg Asp Pro Thr Thr Pro Xaa Thr Arg Ala Ala Trp Glu Thr Val
385                   390                   395                   400
Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr Ala
                 405                   410                   415
Pro Thr Ile Trp Val Arg Met Val Ile Met Thr His Phe Phe Ser Ile
         420                   425                   430
Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met Tyr
         435                   440                   445
Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu
    450                   455                   460
Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His
465                   470                   475                   480
```

```
Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro Pro
                485                 490                 495
Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile
            500                 505                 510
Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp
        515                 520                 525
Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg
    530                 535                 540
Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Gly Asp Ile
545                 550                 555                 560
Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Leu Cys Leu
                565                 570                 575
Leu Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg
            580                 585                 590
```

<210> 2
<211> 1776
<212> DNA
<213> Artificial Sequence

<220>
<223> modified NS5B

<221> variation
<222> (3)...(3)
<223> n = A or T

<221> variation
<222> (9)...(9)
<223> n = C or A

<221> variation
<222> (13)...(13)
<223> n = A or T

<221> variation
<222> (15)...(15)
<223> n = A or C

<221> variation
<222> (21)...(21)
<223> n – A or G

<221> variation
<222> (24)...(24)
<223> n = C or G

<221> variation
<222> (28)...(28)
<223> n = T or C

<221> modified_base
<222> (30)...(30)
<223> n = G or C

<221> variation

<222> (33)...(33)
<223> n = C or A

<221> variation
<222> (71)...(71)
<223> n = A or G

<221> variation
<222> (83)...(83)
<223> n = G or T

<221> variation
<222> (1174)...(1174)
<223> n = A or C

<400> 2
tcnatgtcnt acncntggac nggngccntn atnacaccat gtgggcccga agaggagaag 60
ttaccgatca nccctctgag taattcgctc atncggttcc ataataaggt gtactccaca 120
acctcgagga gtgcctctct gagggcaaag aaggtgactt ttgacagggt gcaggtgctg 180
gacgcacact atgactcagt cttgcaggac gttaagcggg ccgcctctaa ggttagtgcg 240
aggctcctca cggtagagga agcctgcgcg ctgaccccgc cccactccgc caaatcgcga 300
tacggatttg gggcaaaaga ggtgcgcagc ttatctagga gggccgttaa ccacatccgg 360
tccgtgtggg aggacctcct ggaagaccaa cataccccaa ttgacacaac tatcatggct 420
aaaaatgagg tgttctgcat tgatccaact aaaggtggga aaaagccagc tcgcctcatc 480
gtataccccg accttggggt cagggtgtgc gaaaagatgg ccctctatga catcgcacaa 540
aagcttccca aagcgataat ggggccatcc tatgggttcc aatactctcc cgcagaacgg 600
gtcgatttcc tcctcaaagc ttggggaagt aagaaggacc caatgggggtt ctcgtatgac 660
acccgctgct ttgactcaac cgtcacggag agggacataa gaacagaaga atccatatat 720
caggcttgtt ctctgcctca agaagccaga actgtcatac actcgctcac tgagagactt 780
tacgtaggag ggcccatgac aaacagcaaa gggcaatcct gcggctacag gcgttgccgc 840
gcaagcggtg ttttcaccac cagcatgggg aataccatga catgttacat caaagccctt 900
gcagcgtgta aggctgcagg gatcgtggac cctgttatgt tggtgtgtgg agacgacctg 960
gtcgtcatct cagagagcca aggtaacgag gaggacgagc gaaacctgag agctttcacg 1020
gaggctatga ccaggtattc cgcccctccc ggtgaccttc ccagaccgga atatgacttg 1080
gagcttataa catcctgctc ctcaaacgta tcggtagcgc tggactctcg gggtcgccgc 1140
cggtacttcc taaccagaga ccctaccact ccantcaccc gagctgcttg ggaaacagta 1200
agacactccc ctgtcaattc ttggctgggc aacatcatcc agtacgcccc cacaatctgg 1260
gtccggatgg tcataatgac tcacttcttc tccatactat tggcccagga cactctgaac 1320
caaaatctca attttgagat gtacggggca gtatactcgg tcaatccatt agacctaccg 1380
gccataattg aaaggctaca tgggcttgaa gccttttcac tgcacacata ctctccccac 1440
gaactctcac gggtggcagc aactctcaga aaacttggag cgcctcccct tagagcgtgg 1500
aagagtcggg cgcgtgccgt gagagcttca ctcatcgccc aaggagcgag ggcggccatt 1560
tgtggccgct acctcttcaa ctgggcggtg aaaacaaagc tcaaactcac tccattgccc 1620
gaggcgagcc gcctggattt atccgggtgg ttcaccgtgg gcgccggcgg gggcgacatt 1680
tatcacagcg tgtcgcatgc ccgaccccgc ctattactcc tttgcctact cctacttagc 1740
gtaggagtag gcatctttttt actccccgat cgatga 1776

<210> 3
<211> 1394
<212> PRT
<213> Artificial Sequence

<220>
<223> modified NS3-5A

<221> VARIANT
<222> (1215)...(1215)

<223> Xaa = asparagine or serine

<221> VARIANT
<222> (904)...(904)
<223> Xaa = valine or alanine

<400> 3
```
Met Ala Pro Ile Thr Ala Tyr Ser Gln Gln Thr Arg Gly Leu Leu Gly
 1               5                  10                  15
Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
            20                  25                  30
Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
        35                  40                  45
Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
    50                  55                  60
Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
65                  70                  75                  80
Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
            85                  90                  95
Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
            100                 105                 110
Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
        115                 120                 125
Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
    130                 135                 140
Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
145                 150                 155                 160
Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
                165                 170                 175
Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
            180                 185                 190
Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly
        195                 200                 205
Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
    210                 215                 220
Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
225                 230                 235                 240
Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
                245                 250                 255
Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
            260                 265                 270
Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
        275                 280                 285
Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
    290                 295                 300
Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
305                 310                 315                 320
Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
                325                 330                 335
Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
            340                 345                 350
Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
        355                 360                 365
Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
    370                 375                 380
Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
385                 390                 395                 400
```

Ile Pro Thr Ile Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met
                405   410   415
Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys
                420   425   430
Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu
                435   440   445
Thr Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly
           450   455   460
Arg Thr Gly Arg Gly Arg Met Gly Ile Tyr Arg Phe Val Thr Pro Gly
465   470   475   480
Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr
                485   490   495
Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val
                500   505   510
Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp
                515   520   525
His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp
           530   535   540
Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr
545   550   555   560
Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro
                565   570   575
Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr
                580   585   590
Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn
           595   600   605
Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met
610   615   620
Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly
625   630   635   640
Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val
                645   650   655
Ile Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp
                660   665   670
Arg Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser
           675   680   685
His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys
           690   695   700
Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala
705   710   715   720
Ala Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp
                725   730   735
Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly
                740   745   750
Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe
           755   760   765
Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe
           770   775   780
Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala
785   790   795   800
Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser
                805   810   815
Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala
                820   825   830
Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met
           835   840   845
Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro

```
        850                    855                        860
Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His
865                    870                    875                    880
Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala
                       885                    890                    895
Phe Ala Ser Arg Gly Asn His Xaa Ser Pro Thr His Tyr Val Pro Glu
            900                         905                    910
Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile
            915                         920                    925
Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser
        930                         935                    940
Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys
945                    950                    955                    960
Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro
                       965                    970                    975
Gln Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly
            980                         985                    990
Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala
            995                         1000                   1005
Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro
    1010                        1015                       1020
Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr
1025                        1030                   1035                   1040
Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala
                       1045                   1050                   1055
Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly
            1060                        1065                   1070
Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro
            1075                        1080                   1085
```